Putting the pieces together again: genes, child maltreatment and psychoanalysis

The 33rd Annual Daniel S. Prager Lecture
David Reiss, MD
Yale Child Study Center
May 1, 2014
Robert Plomin
Comparison of MZ (identical) and DZ (fraternal) twins: comparing heights within twin pairs (contrived data)

1.00  
Sibling A   Sibling B

0.50  
Sibling B   Sibling A

MZ twins
DZ twins
Summary of data from Plomin’s studies Twins reared together (T) and Apart (A)
MZ = monozygotic  DZ = dizygotic
Summary of Plomin’s data

Correlation coefficients

Between-sibling differences:
Nonshared environment + error

Between-family differences:
Shared environment

MZT  MZA  DZT  DZA  Unrel sib
Summary of Plomin’s data

Correlation coefficients

Shared family en: SES, Neighborhood decay, maternal depression
MIRROR IMAGE TWIN STUDIES: Adolescents-as-twins study (NEAD) vs parents-as-twins study (TOSS)

### Genetic relatedness

<table>
<thead>
<tr>
<th>Sib type (P-P)</th>
<th>Genetic relatedness</th>
</tr>
</thead>
<tbody>
<tr>
<td>254 MZ moms</td>
<td>100%</td>
</tr>
<tr>
<td>284 DZ moms</td>
<td>50%</td>
</tr>
<tr>
<td>128 MZ dads</td>
<td>100%</td>
</tr>
<tr>
<td>183 DZ dads</td>
<td>50%</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Sib type (A-A)</th>
<th>Genetic relatedness</th>
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</thead>
<tbody>
<tr>
<td>93 MZ</td>
<td>100%</td>
</tr>
<tr>
<td>99 DZ</td>
<td>50%</td>
</tr>
<tr>
<td>95 FS-non div</td>
<td>50%</td>
</tr>
<tr>
<td>182 FS-step</td>
<td>50%</td>
</tr>
<tr>
<td>109 HS-step</td>
<td>25%</td>
</tr>
<tr>
<td>130 Blended step</td>
<td>0%</td>
</tr>
</tbody>
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MIRROR IMAGE TWIN STUDIES: Adolescents-as-twins study (NEAD) vs parents-as-twins study (TOSS)

Parent Spouse

Sib type (P-P) Genetic relatedness
254 MZ moms 100%
284 DZ moms 50%
128 MZ dads 100%
183 DZ dads 50%

Parent Spouse

Sib type (A-A) Genetic relatedness
93 MZ 100%
99 DZ 50%
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### Adolescent antisocial behavior

<table>
<thead>
<tr>
<th>OBSERVER CODE</th>
<th>PARENT AND CHILD REPORT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disruptive, rude, aggressive, coercive behavior</td>
<td>Trouble in school, skipped school mean, bully.</td>
</tr>
<tr>
<td>school behavior</td>
<td>Stole, lied, cheated</td>
</tr>
<tr>
<td>brief, in home video</td>
<td>home and neighborhood</td>
</tr>
</tbody>
</table>
Illustration of within sib pair correlations for estimating genetic influence on antisocial behavior.

Sibling A

MZ
A’s antisocial behavior

DZ
A’s antisocial behavior

Sibling B

B’s antisocial behavior

B’s antisocial behavior
Antisocial behavior: Mother, father, child and observer reports
Numbers on vertical axis are intraclass correlations within sibships

Heritability = 67%
Environmentality: Shared = 12%  Nonshared = 21%
<table>
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<tr>
<th>OBSERVER CODES</th>
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<tr>
<td>Anger and rejection</td>
<td>Disagreement</td>
</tr>
<tr>
<td>Coercion</td>
<td>Punitiveness</td>
</tr>
<tr>
<td>Conflict</td>
<td>Yielding to coercion</td>
</tr>
<tr>
<td></td>
<td>Open conflict</td>
</tr>
<tr>
<td></td>
<td>Verbal aggression</td>
</tr>
</tbody>
</table>
Illustration of within sibling correlations for detecting genetic influences on mother’s negativity

Sibling A | Sibling B
---|---
**MZ**
- mother’s negativity to sib A
- mother’s negativity to sib B

**DZ**
- mother’s negativity to sib A
- mother’s negativity to sib B
Mother’s negativity towards child: within sibship correlations across sibling types.
Numbers on vertical axis are intraclass correlations within sibships

Heritability = 59%
Environmentality: Shared = 15% Nonshared = 26%
Illustration of *cross-variable*, within-sib pair correlations for detecting overlap of genetic influences

Sibling A

- mother’s negativity to sib A
- A’s anti-social behavior

Sibling B

- mother’s negativity to sib B
- B’s anti-social behavior
Overlapping genetic influences on mother’s negativity and adolescent antisocial behavior: comparing *cross variable*, within sib pair correlations

Phenotypic correlation = .59

- 68% of this corr. is attributable to G
- 27% of this corr. is attributable to SE
Evocative gene-environment correlations: null hypothesis, family effects and child effects versions

parent influences

Mother-child negative interaction

(heritable & evocative child characteristic)

G_a

Adolescent antisocial behavior

child evokes

FAMILY EFFECTS

CHILD EFFECTS

NULL HYPOTHESIS
Early Growth & Development Study
n=361 expanded to n = 561

BIRTH PARENTS
SUDs and related disorders

Birth Mother
Birth Father

ADOPTIVE PARENTS
Parenting in the context of depression, marital problems and economic worries

Adoptive Mother
Adoptive Father

ENVIRONMENTAL INFLUENCES

ADOPTED CHILDREN
Externalizing and internalizing problems

Genetic Influences

Adopted Child
Early Growth & Development Study

BIRTH PARENTS
- SUDs and related disorders

ADOPTIVE PARENTS
- Parenting in the context of depression, marital problems and economic worries

ADOPTED CHILDREN
- Externalizing and internalizing problems

Genetic Influences

Environmental moderation
I can’t understand my baby
I can’t make my baby look at me
I don’t know what games and toys my baby likes
My kid struggles over bed time
Baby sitters are hard to find
Always cleaning up messes of toys and food
When my child misbehave I raise my voice and yell
When I am under stress I am picky and on my child’s back

*Items slightly paraphrased from D. S. Arnold (1993), KA Crnic (1990) and DM Teti (1991)*
Early Growth & Development Study

**BIRTH PARENTS: SUDs and related disorders**

**Genetic Influences**

**Evocative influences**

**Environmental Influences**

**ADOPTED CHILDREN**

- Internalizing and externalizing problems

**ADOPTIVE PARENTS**

- Parenting in the context of depression, marital problems and economic worries
Prospective adoption study

Adoptive Parents in ADVERSE CONTEXT

Adoptive Parents in FAVORABLE CONTEXT
Child’ high and low genetic risk for externalizing disorders and adoptive parents’ hostile parenting

Contrived data

BM high externalizing

BM low externalizing

Child externalizing problems

adoptive parents’ hostile parenting
Children high and low genetic risk for externalizing disorders and adoptive parents’ marital satisfaction (n = 561)

Source: P. Fearon, submitted
Birth mother externalizing

Marital distress

BM externalizing x Marital distress

Adoptive mother vexation (9-27 mos.)

Child behavior Problems (27 mos.)

.03

.23

.16

.42
David Barker  1938-2013
Low birth weight and hypertension

In their study of 77 men aged 28 Professor Gerhard Gennser and colleagues found a relation between increased diastolic blood pressure and low birth weight after a previous low birth weight (28 March 1488)

D J P BARKER
C OSMOND

MRC Environmental Epidemiology Unit,
Southampton General Hospital,
Southampton SO9 4XY
Long term impact of restricted fetal growth: Standardized mortality ratios due to ischemic heart disease and chronic, obstructive pulmonary disease
7991 men born in Hertfordshire between 1911-1930
source: DJP Barker et al 1989

![Graph showing standardized mortality ratios vs birth weight for ischemic heart disease and obstructive lung disease.](image-url)
Critical evidence for programming: the added risk of “catch-up” growth for death from coronary artery disease

3641 men born in Helsinki between 1924 and 1933

Hazard ratios (deaths/unit time compared to Finnish avg. for age and birth year)

Source: JG Erikson, 1999
Confirmation of the effects of fetal growth restriction in a *rat model*: birth weight and adult (12 week) systolic BP

*Source*: MF Shreuder et al, 2006

![Graph showing relationship between birth weight (grams) and systolic BP (mmHg)]
Low birth weight and depression in teenage girls (n= 1420)
n=81 low birth weight(< 5.5 lbs)
Source: Great Smoky Mountain Study EJ Costello, 2007

(Post natal sexual abuse, physical abuse neglect, parental mental illness, stressful events)
Caroline Bedell Thomas, MD 1904-1997
Cumulative probability of coronary heart disease (MH, angina or other CHD): 1131 white, male Hopkins med students with annual follow-up (The Johns Hopkins Precursor Study Caroline Thomas original PI JHMS Classes of 1948-1961)

source MM Kittleson, 2006
Prospective study of childhood adversity before 11 and adult risk of illness at age 32: 972 in the Dunedin, NZ study

source: A. Danese & T. Moffitt, 2009

Note: At least 3 of 1) overwt; 2) hi BP; 3) hi cholest.; 4) lo high density LP; 5) hi HbA1c; 6) low 0₂ consumption
Documented child abuse and neglect before age 11 and objective signs of illness risk at age 40

source: C Widom 2012

* HbA1c > 6%

Malnutrition
  (BMI/lymphocyte/albumin)

Controls:
  - age
  - gender
  - race
  - childhood SES
  - adult SES
  - smoking
  - substance abuse
  - depression/PTSD

* p < .05  ** p < .01 in comparisons to 237 controls
Experimental assignment to rearing conditions: health outcomes

source: S. Suomi and colleagues (see Conti, G Suom S, Heckman J et al, 2012)

Timeline

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- Nursery reared
- Mother rearing continued
- Group housing
- Observations of impaired medical and behavioral health
Early childhood adversity and subsequent illness
source: Conti, G et al 2012

* Peer exposure 2 hr/d in first year
Accelerated telomere shortening in response to life stress

Elissa S. Epel*, Elizabeth H. Blackburn*, Jue Lin*, Firdaus S. Dhabhar†, Nancy E. Adler*, Jason D. Morrow†, and Richard M. Cawthon†

*Department of Psychiatry, University of California, San Francisco, CA 94143; †Department of Biochemistry and Biophysics, University of California, San Francisco, CA 94143; ‡Department of Oral Biology, College of Dentistry, and Department of Molecular Virology, Immunology, and Medical Genetics, College of Medicine, Ohio State University, Columbus, OH 43210; §Department of Medicine and Pharmacology, Vanderbilt University School of Medicine, Nashville, TN 37232; and †Department of Human Genetics, University of Utah, 15 North 2030 E Street, Room 2100, Salt Lake City, UT 84112

Contributed by Elizabeth H. Blackburn, September 28, 2004
Telomerase
39 care giving mothers
19 mothers of healthy children

Telomere length

Telomerase levels
Telomere length and adult reports of maltreatment “when I was growing up.”

Source: A Tryka, 2010
Experimental assignment to rearing conditions: health outcomes

source: S. Suomi and colleagues (see Conti, G Suom S, Heckman J et al, 2012)

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- Nursery reared
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Observations of impaired medical and behavioral health
Early life social conditions

Suomi

- Down regulated
- Up regulated

- Inflammation
- Cell growth/differentiation
- Transcription control
- Immunoglobulin production
- Type I interferon antiviral response
Adolescent Twin Study
   Robert Plomin, IOP (UK)
   Mavis Hetherington, UVa
   Jenae Neiderhiser, Penn State
   Jody Ganiban, GWU

Adoption Study
   Leslie Leve, U Oregon
   Jenae Neiderhiser, Penn State
   Danny Shaw, Pitt
   Jody Ganiban, GWU
   Pasco Fearon, UCL (UK)

NIH/NIA Project on early adversity ("Reversibility")
   Stephen Suomi, NICHD
   Richard Suzman, NIA/BSR
   Lisbeth Nielsen, NIA/BSR
Maternal negative and adolescent antisocial behavior: contemporaneous analysis at age 12.5
Common genetic influence on association between prior parenting and subsequent antisocial behavior (controlling for stability, contemporaneous associations and adolescent asb -> maternal negativity)

Maternal negativity

Adolescent antisocial behavior

11.5 mean age of adolescent

14.5

A

.39

.45
The relationship between child temperament and maternal negativity and conflict

Source: J Ganiban, 2011

Imperturbable parent

Perturbed parent

Variance of mn attributable to G (unstandardized)
Parental behavior and expression of genetic influence on antisocial behavior


- Harsh parenting
- Warm parenting

These include the imperturbable parents

LO  Directly observed parental behavior
HI  Proportion of genetic influence on antisocial behavior
Parental behavior and expression of genetic influence on disinhibited behavior

Source: J. Ulbricht, 2013
Evocative rGE on Child ADHD Symptoms

(G. Harold et al., JCPP in press)

Genetically Related

- Biological Mother ADHD sx

Adoptive Mother-to-Child Hostility

- Child Impulsivity/Activation

Genetically Unrelated

Adoptive Mother ADHD sx

- Child ADHD sx (father report)

27 months 4.5 years 6 years
Child’s genetic risk for SUDs and mother’s depression/anxiety n = 361

BM high
eexternalizing

BM low
eexternalizing

9 mos. Low Adoptive Mother depression/anxiety High

*Attention frustration task

Source L. Leve, Child Develop. ‘10
Children at low and high risk for SUD (+) & adopted mothers structured parenting (n = 361)

Low Adoptive mother structured parenting* High

* Coded videotape

Source: L Leve, JAACAP, 2009
Children at low and high risk for SUD (+) & adopted fathers structured parenting (n = 95)

- **BF low internalizing/externalizing**
- **BF high internalizing/externalizing**

Source: L Leve, JAACAP, 2009